

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 866

[Docket No. 2005N-0081]

Medical Devices; Immunology and Microbiology Devices; Classification of the Automated Fluorescence in situ Hybridization Enumeration Systems

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is classifying automated fluorescence in situ hybridization (FISH) enumeration systems into class II (special controls). The special control that will apply to the device is the guidance document entitled “Class II Special Controls Guidance Document: Automated Fluorescence *in situ* Hybridization (FISH) Enumeration Systems.” The agency is classifying the device into class II (special controls) in order to provide a reasonable assurance of safety and effectiveness of the device. Elsewhere in this issue of the **Federal Register**, FDA is publishing a notice of availability of a guidance document that is the special control for this device.

DATES: This rule becomes effective [*insert date 30 days after date of publication in the Federal Register*]. The classification was effective December 13, 2004.

FOR FURTHER INFORMATION CONTACT: Maria Chan, Center for Devices and Radiological Health (HFZ-440), Food and Drug Administration, 2098 Gaither Rd., Rockville, MD 20850, 240-276-0493, ext. 130.

SUPPLEMENTARY INFORMATION:

I. Background

In accordance with section 513(f)(1) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360c(f)(1)), devices that were not in commercial distribution before May 28, 1976, the date of enactment of the Medical Device Amendments of 1976, generally referred to as postamendments devices, are classified automatically by statute into class III without any FDA rulemaking process. These devices remain in class III and require premarket approval, unless and until the device is classified or reclassified into class I or II, or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the act, to a predicate device that does not require premarket approval. The agency determines whether new devices are substantially equivalent to previously marketed devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807) of FDA's regulations.

Section 513(f)(2) of the act provides that any person who submits a premarket notification under section 510(k) of the act for a device that has not previously been classified may, within 30 days after receiving an order classifying the device in class III under section 513(f)(1) of the act, request FDA to classify the device under the criteria set forth in section 513(a)(1) of the act. FDA shall, within 60 days of receiving such a request, classify the device by written order. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the **Federal Register** announcing such classification (section 513(f)(2) of the act).

In accordance with section 513(f)(1) of the act, FDA issued an order on October 1, 2004, classifying the VYSIS AUTOVYSION SYSTEM in class III,

because it was not substantially equivalent to a device that was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, or a device which was subsequently reclassified into class I or class II. On October 13, 2004, Vysis, Inc. submitted a petition requesting classification of the VYSIS AUTOVYSION SYSTEM under section 513(f)(2) of the act. The manufacturer recommended that the device be classified into class II.

In accordance with section 513(f)(2) of the act, FDA reviewed the petition in order to classify the device under the criteria for classification set forth in section 513(a)(1) of the act. Devices are to be classified into class II if general controls, by themselves, are insufficient to provide reasonable assurance of safety and effectiveness, but there is sufficient information to establish special controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. After review of the information submitted in the petition, FDA determined that the VYSIS AUTOVYSION SYSTEM can be classified in class II with the establishment of special controls. FDA believes these special controls, in addition to general controls, will provide reasonable assurance of safety and effectiveness of the device.

The device is assigned the generic name automated FISH enumeration system. It is identified as a device that consists of an automated scanning microscope, image analysis system, and customized software applications for FISH assays. This device is intended for in vitro diagnostic use with FISH assays as an aid in the detection, counting, and classification of cells based on recognition of cellular color, size, and shape, and in the detection and enumeration of FISH signals in interphase nuclei of formalin-fixed, paraffin-embedded human tissue specimens.

FDA has identified the risks to health associated with this type of device as inaccurate results that could lead to improper patient management. Improper patient management, which includes misdiagnosis and improper treatment, could result from failure of the test to perform as indicated or error in interpretation of results. A falsely low fluorescence signal count, or false negative, could contribute to a delay in detecting the disease, disease recurrence, disease prognosis, or a false indication of response to therapy. A falsely high fluorescence signal count, or false positive, could contribute to unnecessary monitoring, inappropriate treatment decisions, or failure to treat adequately. In addition, use of assay results to adjust a treatment regimen without consideration of other clinical factors could pose a risk.

The class II special controls guidance document aids in mitigating potential risks by providing recommendations on validation of performance characteristics, including software validation; control methods; reproducibility; and clinical studies. The guidance document also provides information on how to meet premarket (510(k)) submission requirements for the device. FDA believes that following the class II special controls guidance document generally addresses the risks to health identified in the previous paragraph. Therefore, on December 13, 2004, FDA issued an order to the petitioner classifying the device into class II. FDA is codifying this classification by adding § 866.4700.

Following the effective date of this final classification rule, any firm submitting a 510(k) premarket notification for an automated FISH enumeration system will need to address the issues covered in the special controls guidance. However, the firm need only show that its device meets the recommendations

of the guidance, or in some other way provides equivalent assurance of safety and effectiveness.

Section 510(m) of the act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. For this type of device, however, FDA has determined that premarket notification is necessary because FDA's review of the system's key performance characteristics, test methodology and labeling to satisfy requirements of § 807.87(e), will provide reasonable assurance that acceptable levels of performance for both safety and effectiveness will be addressed before marketing clearance. Thus, persons who intend to market this type of device must submit to FDA a premarket notification, prior to marketing the device, which contains information about the automated FISH enumeration system they intend to market.

II. Environmental Impact

The agency has determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

III. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental,

public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this final rule is not a significant regulatory action under the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because classification of these devices into class II will relieve manufacturers of the device of the cost of complying with the premarket approval requirements of section 515 of the act (21 U.S.C. 360e), and may permit small potential competitors to enter the marketplace by lowering their costs, the agency certifies that the final rule will not have a significant impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing “any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any one year.” The current threshold after adjustment for inflation is \$115 million, using the most current (2003) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this final rule to result in any 1-year expenditure that would meet or exceed this amount.

IV. Federalism

FDA has analyzed this final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of

government. Accordingly, the agency has concluded that the rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement is not required.

V. Paperwork Reduction Act of 1995

This final rule contains no collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

VI. Reference

The following reference has been placed on display in the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Petition from Vysis, Inc., dated October 13, 2004.

List of Subjects in 21 CFR Part 866

Biologics, Laboratories, Medical devices.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 866 is amended as follows:

PART 866—IMMUNOLOGY AND MICROBIOLOGY DEVICES

■ 1. The authority citation for 21 CFR part 866 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

■ 2. Section 866.4700 is added to subpart E to read as follows:

§ 866.4700 Automated fluorescence *in situ* hybridization (FISH) enumeration systems.

(a) *Identification.* An automated FISH enumeration system is a device that consists of an automated scanning microscope, image analysis system, and customized software applications for FISH assays. This device is intended for in vitro diagnostic use with FISH assays as an aid in the detection, counting and classification of cells based on recognition of cellular color, size, and shape, and in the detection and enumeration of FISH signals in interphase nuclei of formalin-fixed, paraffin-embedded human tissue specimens.

(b) *Classification*. Class II (special controls). The special control is FDA's guidance document entitled "Class II Special Controls Guidance Document: Automated Fluorescence *in situ* Hybridization (FISH) Enumeration Systems." See § 866.1(e) for the availability of this guidance document.

Dated: March 10, 2005.

Linda S. Kahan,

Deputy Director, Center for Devices and Radiological Health.

[FR Doc. 05-???? Filed ??-??-05; 8:45 am]

BILLING CODE 4160-01-S